

**ABSTRACT**

Methods and compositions are provided for altering the DNA recognition and cleavage characteristics of an endonuclease without prior knowledge of the endonuclease's three-dimensional structure and/or amino acid residues responsible for activity and/or specificity. Methods include subjecting a mutagenized endonuclease gene library to a genetic selection in prokaryotic cells which tolerate the expression of mutated endonuclease and where the endonuclease is active and determining the altered recognition-site specificity for the endonuclease.